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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/056,072	BAZIN ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/4/05; 8/17/05; 2/22/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed on 2/4/2005, has been entered.

Claims 30-44 are pending and being acted upon.

Claims 1-29 have been canceled previously.

2. It appears that applicant's submission on 8/17/05 has placed this application in compliance with the Sequence Rules.

3. The substitute specification in conjunction with applicant's statements filed 8/17/05, has been entered and is in compliance with 37 CFR 1.125(b).

4. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821-1.825
Applicant is required to amend the specification (e.g. see Brief Description of the Drawings, particularly Figures 29-34) to indicate the appropriate SEQ ID NOS.

Applicant is reminded that the following and should amend the specification accordingly (e.g. see page 12 of the instant specification).
The current address of the ATCC is as follows:
American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110-2209

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:
A person shall be entitled to a patent unless --
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 30-32 and 35-37 stand rejected under 35 U.S.C. 102(b) as being anticipated by Xia et al. (Rat Hybridomas and Rat Monoclonal Antibodies, 1990) for the reasons of record.

Applicant's arguments, filed 2/4/05 and the examiner's rebuttal are essentially the same of record.

Upon reconsideration of the Decision on Appeal by the BPAI, mailed 7/31/2003, the previous rejection of claims 35-37 has been withdrawn.

Applicant asserts that the burden is upon the examiner show that Xia et al. discloses all of the elements and limitations of applicant's claimed antibody, that is, an antibody that binds the same epitope on human lymphocytes as the antibody produced by the cell line deposited as ATCC HB 11423.

Applicant appears to assert that Xia et al. is limited to standard procedures of producing anti-CD2 antibodies, which would resulted in producing a myriad of anti-CD2 antibodies, with no evidence that the ordinary artisan would be able to obtain and claimed antibody specificity from a wide variety of other possible antibodies.

Again, it appears that applicant is asserting that the totality of the references, including the Bierer Declaration, indicate that the characteristics disclosed by Xia et al. are not sufficient to identify LO-CD2 in a manner that distinguishes LO-CD2 from CD2 antibodies as a class or enables the ordinary artisan to identify antibodies which binds to the same epitope as the antibody produced by the deposited cell line.

In contrast to appellant's arguments, Xia et al. teach the LO-CD2a-specificity and rely upon a number of characteristics to distinguish this specificity (see entire document, including Tables 1-6 and Figures 1-4), including distinguishing the LO-CD2 specificity from other CD2-specific antibodies (see page 320, paragraphs 1-3).

Here in Xia et al.; the Tables and Figures provide for a profile of binding specificities and functional properties both in a quantitative and qualitative manner. For example, Tables 1-4 and Figures 1-4 provide for reactivity patterns of antibodies that provide for intensity of binding in addition to binding specificity.

Here, the LO-CD2 antibody specificity is compared with another anti-CD2 antibody specificity, namely the OKT11/T11 antibody (See Tables and Figures).

Xia et al. discloses that reactivity patterns of LO-CD2 antibody and OKT11 exhibit similarities; they are not considered identical. See page 320, paragraph 1.

Here, the difference between LO-CD2 and OKT11 is that LO-CD2 always show a weaker reaction with T lymphocytes than T11 and that LO-CD2 did not react with T cell line CEM, while OKT11 did.

Xia et al. distinguish the epitope recognized by another CD2 antibody, namely D66, based upon functional characteristics of blocking E-rosette formation. See page 320, paragraph 2.

LO-CD2 was also compared with non-CD2-specific antibodies, wherein the effect of LO-CD2 was in sharp contrast to that of CD25-specific antibodies. See page 320, paragraph 4.

Section 4 of the Bierer Declaration. asserts that reactivity patterns in Figures 1A/1B is not statistically different from another CD2 antibody, namely OKT11.

However, as pointed out above; Xia et al. do not rely upon Figures 1A/1B alone to distinguish LO-CD2 from OKT11. Here, the difference between LO-CD2 and OKT11 is that LO-CD2 always show a weaker reaction with T lymphocytes than T11 and that LO-CD2 did not react with T cell line CEM while OKT11 did.

Section 16 of the Bierer Declaration relies upon the Third International Workshop and Conference on Human Leukocyte Differentiation Antigens, 1986 (page 149) to indicate that several CD2 antibodies which did not react with CEM cells, did react with MOLT4 cells, HPB-ALL cells and Jurkat cells, whereby the reactivity patterns of Table 4 is not unique to LO-CD2.

It appears that even among these CD2-specific antibodies referred to Table 1 (page 149) of the Third International Workshop; these antibodies do not have the same or identical characteristic profiles that these profiles can be distinguished from all of the characteristics of the LO-CD2a-specificity set forth in Xia et al.

Also, in contrast to applicant's assertions and as noted in the Decision on Appeal by the BPAI, mailed 7/31/2003;

Xia et al. teach the LO-CD2a antibody, subsequently deposited as ATCC HB 11423, teaches the methodology of producing antibodies and hybridomas, and teach the reactivity pattern of LO-CD2a with normal and leukemic cells.

Also, as noted on page 8 the Decision on Appeal by the BPAI, mailed 7/31/2003;
"As a whole, we are not persuaded by either appellant's Brief or the Bierer declaration. While the Brief relies heavily on the Bierer declaration, Bierer discusses Xia's tables individually, and fails to address the significance of the data when viewed as a whole. As the examiner explains (Answer, page 9), "it is the totality of the reactivity patterns and functional characteristics, clearly disclosed in Xia et al. that serves to distinguish the LO-CD2[a] antibody specificity over the prior art and not just binding to one cell line or even a few binding characteristics."

Again, it is the totality of the reactivity patterns and functional characteristics clearly disclosed in Xia et al. that serves to distinguish the LO-CD2a antibody specificity over the prior art and not just binding to one cell line or even a few binding characteristics.

Given all of the criteria of the anti-LO-CD2a antibody specificity clearly taught and enabled by the prior art Xia et al. teaching; the ordinary artisan would have been enabled to making and using antibodies which bind the same LO-CD2a epitope encompassed by the claimed invention.

While the characteristics disclose by the prior art may be common to certain classes of CD2-specific antibodies, this reference clearly distinguishes the LO-CD2a antibody specificity from other CD2-specific antibodies, including providing a profile of a number of characteristics and comparisons for antibodies that bind the same epitope as the LO-CD2a antibody.

Therefore, claims 30-32, 35-40 and 43 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Xia et al. (Rat Hybridomas and Rat Monoclonal Antibodies, 1990).

With respect to applicant's assertions that nothing in the record would indicate that because LO-CD2a antibody produced by Xia et al. would necessarily be produced again by the referenced methods,
applicant is reminded that the rejection is not directed towards the LO-CD2a antibody per se.
Applicant is reminded that the prior art rejection is based upon antibodies that bind the same epitope as the LO-CD2a antibody rather than based upon producing the LO-CD2a antibody itself or other LO-CD2a-specific antibodies with the same exact chemical structure as the LO-CD2a antibody.

Appellant's arguments have not been found persuasive.

Xia et al. teach the LO-CD2a-specificity, including hybridomas and methods of making said antibodies and hybridomas of the instant invention (see entire document and page 312 for example).

See the Examiner's Answer, mailed 8/24/00, for a more complete analysis of applicant's arguments and the examiner's rebuttal.

8. New Ground of Rejection

Claims 30-31 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Olive et al. (Leucocyte Typing III, edited by McMichael et al., Oxford University Press, Oxford, 1987; see pages 148-153) and as further evidenced by Denning et al. (Leucocyte Typing III, edited by McMichael et al., Oxford University Press, Oxford, 1987; see pages ~~148~~ 144-147) and Xu et al. (Clin. Exp. Immunol. 138: 476-483, 2004).

10/30/06 PV

Olive et al. teach the functional activity of CD2 panel antibodies, including the classification of the Workshop CD2 panel of antibodies as well as the 35.1 anti-CD2 antibody.

Given the CD2 panel of anti-CD2 antibodies, including classifying the panel of anti-CD2 antibodies into different groups such as $T11_1$, $T11_2$ and $T11_3$ antibodies (e.g. see Table 4 on page 152), either specific antibodies taught in the prior art or $T11_1$-, $T11_2$- and/or $T11_3$ – specific antibodies would have had the inherent property of binding the same epitope as the LO-CD2a-specific antibodies of the claimed invention.

Comparison of the instant products with prior art is difficult since the Office is not equipped to manufacture the claimed product and/or prior art products that appear to be related and conduct comparisons. The burden is on the applicant to establish a patentable distinction between the claimed and referenced anti-CD2 antibodies. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

With respect to the particular prior art 35.1 anti-CD2 specificity, it is noted that the antibody name of 35.1 is the same as the Workshop No. 448 antibody.
See Table 4 on page 146 of Denning et al.
Xu et al. acknowledged that the antibody 35.1 competes with the LO-CD2a-specific antibody BTI-322 in CD2 binding (see entire document, particularly the first paragraph of the Discussion on page 481).

Given that the 35.1 antibody competes with the LO-CD2a-specific antibody BTI-322 in CD2 binding, members of the panel of the anti-CD2 such as the 35.1 (Workshop No. 448) would have had the inherent properties of binding the same epitope as the LO-CD2a-specific antibodies of the claimed invention.

9. Claims 30-43 are rejected under 35 U.S.C. 103 as being unpatentable over Xia et al. (Rat Hybridomas and Rat Monoclonal Antibodies, 1990) in view of Queen et al. (U.S. Patent No. 5,530,101) or Newman et al. (U.S. Patent No. 5,658,570) and in further view of Guckel et al. (J. Exp. Med., 1991) OR Bromberg et al. (Transplant., 1991) OR Hafler et al. (J. Immunol., 1988) OR Chavin et al. (Transplant., 1992) OR Faustman (U.S. Patent No. 5,283,058) essentially for the reasons of record.

Applicant's arguments in conjunction with the Bierer Declaration filed in priority USSN 08/472,281, now U.S. Patent No. 5,817,311, filed 2/4/05, have been fully considered but have not been found convincing essentially the same of record.

Although applicant's amendment, filed 2/4/05, indicates that the a copy of the Bierer Declarations filed in priority USSN 08/472,281, now U.S. Patent No. 5,817,311, was submitted with the amendment, filed 2/4/05,

no additional Bierer Declaration(s) appears to have been filed with the above-mentioned 2/4/05 Amendment.

Also, see the Transmittal Letter, filed 2/4/05, which does not indicate a filing of an Exhibit or Declaration.

For examination purposes, the Bierer Declaration, filed 1/4/99, in the instant application is the Bierer Declaration under consideration.

Applicant's arguments, including the Bierer Declaration, filed 1/4/99, and the examiner's rebuttal are essentially the same of record.

Applicant's reliance upon the Bierer Declaration has been fully considered but has not been found convincing essentially for the reasons of record, which is addressed above in the rejection under 35 USC 102 as well as in the Decision on Appeal by the BPAI, mailed 7/31/2003.

Applicant relies upon Thurlow et al. (Transplantation 36: 293-297, 1982); however the Thurlow et al. reference does not detract from the teachings of the prior art, including that the prior art relies upon observations and teachings subsequent to the early 1982 Thurlow reference.

While applicant relies upon Giorgi et al. (Transplant. Proc. XV: 639-641, 1983) to indicate that an anti-CD2 antibody was not successful in primates,

Giorgi et al. does indicate that several possible reasons for the differences of the monoclonal antibodies on the treated recipients (see pages 641-642, overlapping paragraph).

Applicant also asserts that there is nothing in the record that would lead one to expect that the claimed compounds could be used in treating patients.

Applicant is reminded that the claims are drawn to antibody compounds and compositions and not to methods of inhibiting transplant rejection.

Further, applicant acknowledges that the prior art does provide for effective antibodies, albeit not as effective as asserted and disclosed on pages 40-43 of the instant specification.

It is not clear what is the intent or point being made by applicant's statement that: "As the examiner was aware, in treating rejection or other T-cell mediated responses, it is virtually impossible to treat within 24 hours of antigen priming."

For example, applicant's instant disclosure is consistent with standard therapeutic regimens of administering an immunosuppressive such as an immunosuppressive antibody at the time of transplantation and for short period thereafter (e.g., see page 19, paragraph 1 of the instant specification).

Further, page 18, paragraph 3 of the instant specification indicates that the scope of the invention is not limited by such amounts, that is, an amounts of at least 1 mg.

Again, applicant is reminded that the claims are drawn to antibody compounds and compositions and not to methods of inhibiting transplant rejection.

Even the intended use recited in the claims is drawn to "an amount effective to inhibit a T-cell mediated immune response" and not inhibiting transplant rejection or inhibiting transplant rejection after onset of rejection, as asserted or indicated by applicant arguments.

Here, too; applicant's reliance upon pages 40-42 of the instant specification is based upon a dosage regimen of 10 mg/day for 12 days or 2.5 / 5 / 10 mg/ day for ten (10) days.

Again, these amounts are not consistent with the recitation of the claims, which do not recite any particular amounts of antibodies, nor with the specification as filed, which indicates that the scope of the invention is not limited by such amounts, that is, an amounts of at least 1 mg (see page 18, paragraph 3 of the instant specification).

Applicant appears to be arguing limitations not claimed or limitations not consistent with the instant disclosure as filed.

The following of record is reiterated for applicant's convenience, wherein the rejection of record provides sufficient motivation and expectation of success in deriving immunosuppressive and therapeutic amounts of anti-CD2 antibodies, including antibodies that bind the same epitope as the LO-CD2a antibody.

The instant claims are drawn to antibodies that bind the LO-CD2a specificity, including chimeric and humanized antibodies, as well as cell that produced said antibodies and methods of making said antibody.

Xia et al. provides a number of phenotypic and functional characteristics that are associated with the LO-CD2a specificity (see entire document). Also, Xia et al. distinguishes the LO-CD2a specificity from other CD2-specific antibodies and clearly discloses that this specificity binds a different epitope from other CD2-specific antibodies (for example, see page 320, paragraphs 1-3). It would have been expected at the time the invention was made that different antibodies would recognize the same conformational epitope, which is the LO-CD2a epitope in the instant case. The prior art clearly set forth numerous features that characterize and enable one of skill in the art at the time the invention was made to make an antibody that binds to the same LO-CD2 epitope specificity as claimed. Xia et al. Differs from the instant claims by not disclosing chimeric or humanized antibodies per se.

Queen et al. teaches the art-known procedures at the time the invention was made to produce chimeric antibodies starting from hybridoma and antibody producing cells (see entire document)..

Similarly, Newman et al. teach the generation of recombinant antibodies including CD2-specific antibodies for various diagnostic and therapeutic uses (see entire document). While it is noted that Newman et al. teaches the use of Old World Monkey portions in the derivation of recombinant antibodies, this reference clearly recognizes the derivation of chimeric and humanized antibodies at the time the invention was made and that CD2 was a desired specificity at the time the invention was made.

One of ordinary skill in the art at the time the invention was made would have generated chimeric or humanized antibodies in order to reduce immunogenicity while retaining high binding affinity for diagnostic and therapeutic purposes as well as the appropriate vectors, host cells, etc. to accomplish the engineering of chimeric and humanized antibodies (see entire documents). Therefore, Queen et al. OR Newman et al. teach that immunoglobulin gene structure and organization were well understood in the art at the time the claimed invention was made and that strategies for cloning the DNAs encoding immunoglobulin variable regions genes were well established in the art at the time the claimed invention was made, as were methods for the production of DNA constructs comprising expression vectors containing DNAs encoding immunoglobulin variable regions. Queen et al. AND Newman et al. differ from the claimed invention by not teaching the LO-CD2a specificity per se, the ordinary artisan would have been motivated to apply the teachings of Queen et al. OR Newman et al. to enable the isolation and construction of chimeric and humanized antibodies that bind the LO-CD2a specificity.

In addition to the LO-CD2a specificity, the instant claims also encompass antibodies that elicit alloantigen specific unresponsiveness. Guckel et al., Bromberg et al., Hafler et al., Chavin et al. and Faustman all teach the art-known potent inhibition of immune responses by blocking or modulating T cell surface receptors such as CD2 that are important in adhesion receptor-signaling (see entire documents, particularly the Introductions and Discussions).

Guckel et al. teach the ability of rat anti-CD2 antibodies to induce T cell unresponsiveness in vitro and in vivo in mice (see entire document). CD2-specific antibody inhibition of transplants and autoimmunity is taught (page 965, column 2, paragraph 2). Guckel et al. Also teach that CD2 modulation was dose and time dependent, whereby a single dose of 0.1 – 5 mg purified antibody resulted in maximal modulation within 24 hours (see page 964, column 1, paragraph 1).

Bromberg et al. teach that anti-CD2 antibodies alter cell-mediated immunity, such as contact sensitivity and CTL responses in vivo by altering the array of cell surface receptors and subsequent responses to antigenic challenge (see entire document). Additional experiments showed a well-defined dose-response relationship between the amount of anti-CD2 administered and subsequent immunosuppression (see Abstract on page 219, column 1). Bromberg et al. also teach the potent immunosuppressive properties of anti-CD2 antibodies for murine allografts and xenografts as well as for primate skin and renal allografts (page 224, column 1, paragraph 1).

Hafler et al. teach that anti-CD2 antibodies inhibit T cell responses in human patients with progressive multiple sclerosis (see entire document). In addition to in vivo effects, the in vivo anti-T cell antibodies infusions could be immunosuppressive as determined by in vitro assays (page 136-137, overlapping paragraph). Patients received 0.2 mg /kg antibody in pharmaceutical compositions (see Materials and Methods mAb Infusions). Hafler et al. also teach that T cell-specific antibodies have been used successfully as immunosuppressive reagents in transplant rejections and autoimmune diseases (see Introduction).

Chavin et al. teaches the efficacy of treating allografts and xenografts in vivo with CD2-specific antibodies (see entire document, particularly the Introduction and Discussion). Prolonged allograft survival correlated with suppression of both CTL and NK activity (page 290, column 1, paragraph 3 and Table 2). Chavin et al. teach that anit-human CD2 antibodies have been used in primate models of allografting and have ben found to be effective immunosuppressive agent and that antihuman CD2 antibody may be quite potent in humans (see page 289, column 2, paragraph 1). Previous and current data demonstrate that anti-CD2 antibodies affects a variety of CD4/CD8 T cell dependent response inducing CTL, contact sensitivity, proliferation, IgG responses, tumor immunity, natural killer cytotoxicity and allograft rejection (see page 290, column 1, paragraph 2). Here, Chavin et al. concludes by stating that the ability of anti-CD2

antibodies to suppress lymphocyte precursors and T and non-T cell responses supports its use for induction therapy in transplantation (page 290, last paragraph).

Faustman teaches methods of inhibiting the rejection of allografts and xenografts with T cell-specific antibodies and antibody fragments including the CD2-specificity (see entire document, including column 5, paragraph 1). Such methods of inhibiting rejection include modifying, eliminating and masking an antigen on the surface of a cell (see entire document, including Abstract). In addition, Faustman teaches perfusion with antibodies is carried out by conventional techniques (see column 10, paragraph 1).

Given the in vitro and in vivo observations of potent blocking of various T cell mediated immune responses, including the induction of antigen specific unresponsiveness,

Given the binding and inhibitory properties of the LO-CD2a-specific antibody, including strongly depressing antigen-induced lymphocyte activation and proliferation taught by Xia et al.; one of ordinary skill in the art would have motivated to employ the LO-CD2a in various biological, diagnostic and therapeutic modalities, as taught by the prior art above. It is noted that Xia et al. acknowledged that the ordinary artisan was motivated to employ monoclonal antibodies as attractive reagents for clinical therapeutic use at the time the invention was made (see Introduction on page 310).

Given the teachings of Guckel et al., Bromberg et al., Hafler et al., Chavin et al. and Faustman of the art-known potent inhibition of immune responses both in vitro and in vivo by blocking or modulating CD2, one of ordinary skill in the art would have had a reasonable expectation of success that the binding and functional properties of the LO-CD2a antibody specificity would have been consistent with such potent antigen-specific immune responses of the prior art anti-CD2 inhibitory antibodies. Given the prior art teachings of antibody compositions for both in vitro and in vivo regimens employing, characterizing and testing antibodies, including anti-CD2 antibodies, the ordinary artisan would have been motivated to place antibodies with the LO-CD2a specificity in composition form, including in amounts effective to inhibit T cell mediated immune responses, as practiced by the prior art (e.g. see Guckel et al., Bromberg et al., Hafler et al., Chavin et al. and Faustman). Also, note that the claimed compositions do not recite a specific amount of anti-LO-CD2a antibodies. It is noted that page 18, paragraph 1 of the instant specification discloses that the scope of the invention is not limited by amounts such as 1 mg. The prior art antibodies including the LO-CD2a antibody specificity do inhibit T cell activation, which is consistent with amounts effective to inhibit T cell mediated immune responses.

It would have prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to generate CD2-specific antibodies including the LO-CD2-specific antibodies to characterize the CD2 specificity and to target said specificity for various biological, diagnostic and therapeutic modalities, as taught by the prior art. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

See the Examiner's Answer, mailed 8/24/00, for a more complete analysis of applicant's arguments and the examiner's rebuttal.

10. New Ground of Rejection.

Claims 30-43 are rejected under 35 U.S.C. 103 as being unpatentable over Olive et al. (Leucocyte Typing III, edited by McMichael et al., Oxford University Press, Oxford, 1987; see pages 148-153) in view of Denning et al. (Leucocyte Typing III, edited by McMichael et al., Oxford University Press, Oxford, 1987; see pages 145-147) in view of Queen et al. (U.S. Patent No. 5,530,101) or Newman et al. (U.S. Patent No. 5,658,570) and in further view of Guckel et al. (J. Exp. Med., 1991) OR Bromberg et al. (Transplant., 1991) OR Hafler et al. (J. Immunol., 1988) OR Chavin et al. (Transplant., 1992) OR Faustman (U.S. Patent No. 5,283,058) essentially for the reasons of record.

Olive et al. teach the functional activity of CD2 panel antibodies, including the classification of the Workshop CD2 panel of antibodies as well as the 35.1 anti-CD2 antibody (see entire document, including Tables 1-5).

Given the CD2 panel of anti-CD2 antibodies, including classifying the panel of anti-CD2 antibodies into different groups such as $T11_1$, $T11_2$ and $T11_3$ antibodies (e.g. see Table 4 on page 152), either specific antibodies taught in the prior art or $T11_1$-, $T11_2$- and/or $T11_3$ – specific antibodies would have had the intrinsic property of binding the same epitope as the LO-CD2a-specific antibodies of the claimed invention.

Further, with respect to the panel of anti-CD2 antibodies, a number of the anti-CD2 antibodies inhibited the T cell responses observed in MLR and CML (e.g. see Table 2).

With respect to the particular prior art 35.1 anti-CD2 specificity, it is noted that the antibody name of 35.1 is the same as the Workshop No. 448 antibody.
See Table 4 on page 146 of Denning et al.

Given the binding and inhibitory properties of the LO-CD2a-specific antibody, including strongly depressing antigen-induced lymphocyte activation and proliferation taught by Olive et al.; one of ordinary skill in the art would have motivated to employ the inhibitory anti-CD2 antibodies in various biological, diagnostic and therapeutic modalities, as taught by the prior art of record as applied to the previous rejection under 35 USC 103 with respect to the teachings of Xia et al. and now similarly is applied to the teachings of Olive et al. and antagonistic anti-CD2 antibodies referenced and taught byt the Workshop.

Given the teachings of Guckel et al., Bromberg et al., Hafler et al., Chavin et al. and Faustman of the art-known potent inhibition of immune responses both in vitro and in vivo by blocking or modulating CD2 as previously applied to the teachings of Xia et al., one of ordinary skill in the art would have had a reasonable expectation of success that the binding and functional properties of the antagonistic anti-CD2 antibodies taught by Olive et al. would have been consistent with such potent antigen-specific immune responses of the prior art anti-CD2 inhibitory antibodies. Given the prior art teachings of antibody compositions for both in vitro and in vivo regimens employing, characterizing and testing antibodies, including anti-CD2 antibodies, the ordinary artisan would have been motivated to place antagonistic anti-CD2 antibodies in composition form, including in amounts effective to inhibit T cell mediated immune responses, as practiced by the prior art (e.g. see Guckel et al., Bromberg et al., Hafler et al., Chavin et al. and Faustman). Also, note that the claimed compositions do not recite a specific amount of anti-LO-CD2a antibodies. It is noted that page 18, paragraph 1 of the instant specification discloses that the scope of the invention is not limited by amounts such as 1 mg. The prior art antibodies including certain antibodies presented in Table 2 of Olive et al. do inhibit T cell activation, which is consistent with providing amounts effective to inhibit T cell mediated immune responses in vivo as well as in vitro.

It would have prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to generate CD2-specific antibodies including the antagonistic anti-CD2 antibodies taught by Olive et al. to characterize the CD2 specificity and to target said specificity for various biological, diagnostic and therapeutic modalities, as taught by the prior art. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. The terminal disclaimer filed on 4/29/96 (Paper No. 14), disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 5,264,554 has been reviewed and is accepted

The terminal disclaimer filed on 2/20/04 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 5,730,979 has been reviewed and is accepted

12. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); In re Van Ornam, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and In re Goodman, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR § 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR § 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR § 3.73(b).

13. Claims 30-44 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 5,951,983.

Although the recitation of the instant and patented claims differ, the patented claims, which are drawn to a humanized version of the LO-CD2a anti-CD2 antibody anticipates or renders obvious the instant claims. Given that the original LO-CD2a antibody was a rat monoclonal antibody, the instantly claimed rat antibody would have been an obvious variant of the patented humanized anti-CD2 antibodies derived from the same starting material. Placing antibodies in composition form for a wide variety of utilities including detection, diagnotistic and therapeutic modalities was obvious to the ordinary artisan at the time the invention was made by the ordinary artisan.

14. Claims 30-44 are directed to an invention not patentably distinct from claims 1-4 of commonly assigned U.S. Patent No. 5,951,983. Specifically, the patented claims, which are drawn to a humanized version of the LO-CD2a anti-CD2 antibody anticipates or renders obvious the instant claims for the reasons set forth above in Section 13.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No. 5,951,983, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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